

CLAIMS

1. A pharmaceutical composition of small-sized, unilamellar liposomes, for parenteral administration of an active compound, comprising: liposomes with an average diameter from about 75 nm to about 300 nm, wherein the unilamellar membrane contains a mixture of saturated lipids, said unilamellar membrane containing at least one lysophospholipid in an amount of about 0,5 mol% to 6.0 mol% regarding the total lipid content, and a therapeutic encapsulated compound included inside said liposomes.
2. A composition according to claim 1, wherein the lysophospholipid is selected from lysophosphatidylcholine, lysophosphatidylinositol, lysophosphatidylserine and lysophosphatidic acid or combinations thereof.
3. A composition according to claim 1, wherein the saturated lipids are selected from phosphatidylcholine, cholesterol, phosphatidylethanolamine, phosphatidylinositol, phosphatidylglycerol, natural phosphatidylcholine (soy and/or egg), distearoyl phosphatidylethanolamine derivatized with O - methylated polyethyleneglycol 750-5000, dipalmitoyl phosphatidylethanolamine derivatized with O-methylated polyethyleneglycol 750-5000 or combinations thereof.
4. A composition according to claim 3, wherein distearoyl phosphatidylethanolamine is derivatized with O-Methyl-polyethylene-glycol 2000
5. A composition according to claim 3, wherein dipalmitoyl phosphatidyl ethanolamine is derivatized with O-methyl-polyethylene-glycol 2000
6. A composition according to claim 1, wherein the active principle is a cytotoxic agent.
7. A composition according to claim 6, wherein the

cytotoxic agent is selected from anthracyclenic antibiotics, taxanes and platinum salts.

8. A composition according to claim 7, wherein the anthracyclenic antibiotic is selected from the group consisting in doxorubicin, epirubicin and daunorubicin and pharmaceutically acceptable salts thereof.

9. A pharmaceutical composition of unilamellar, small sized liposomes for parenteral administration of an active compound, according to claim 1, comprising:
liposomes with an average diameter from about 75 nm to about 300 nm, wherein said unilamellar membrane contains a mixture of saturated lipids, comprising at least one lysophospholipid in an amount of about 0,5 mol% to about 6,0 mol% related to the total lipid content, and encapsulated doxorubicin inside said liposomes in a ratio of about 8,5% by weight to about 11,5% by weight related to the total weight of lipids in the liposomes.

10. A method of preparing a composition according to claim 1, comprising the steps of: forming liposomes from a solution containing saturated lipids and at least a lysophospholipid in an amount of about 0,5 mol% and 6,0 mol% regarding the total lipid content, and evaporation to dryness; taking the film up in aqueous solution; submitting the foregoing solution to freezing and thawing cycles extruding through membranes of decreasing pore up to a membrane of 50 nm pore, obtaining liposomes with an average diameter of about 75 nm to about 300 nm, dialyzing the liposome suspension, and mixing the dialyzed liposome suspension with a solution of the active compound.

11. A method according to claim 10, wherein the lysophospholipid is selected among lysophosphatidylcholine, lysophosphatidylinositol, lysophosphatidylserine and lysophosphatidic acid.

12. A method of preparing a composition of claim 9, comprising the steps of: forming liposomes from a solution containing saturated lipids and at least a lysophospholipid in an amount of about 0,5 mol% to 6,0 mol% regarding the total lipid content, and evaporating to dryness; taking the film up in a solution of an ammonium salt; submitting the foregoing solution to freezing and thawing cycles extruding through membranes of decreasing pore up to a membrane of 50 nm pore, obtaining liposomes with an average diameter of about 75 nm to about 300 nm; dialyzing the liposome suspension against an aqueous solution without ammonium ions; mixing the dialyzed liposome suspension with a solution of about 50 mM to about 200 mM of a soluble calcium salt and a solution of doxorubicin at a concentration of about 2 to about 30 mg/ml, obtaining a percentage of more than 80% of encapsulation of doxorubicin.
13. A method according to claim 12, wherein the calcium salt is calcium chloride.
14. A method according to claim 12 or 13, wherein the volume ratio of calcium chloride solution to doxorubicin solution is of 1:10 (v:v).
15. A method according to claim 12, wherein the percentage of encapsulated doxorubicin increases between 20 to 70% in the presence of calcium chloride, compared to a method which does not use calcium chloride.